

Second Heart Sound in Pulmonary Hypertension

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The clinical diagnosis of pulmonary hypertension may be difficult. Atrial systolic ('a') waves in the venous pulse are an inconstant finding; abnormal right ventricular movement may be absorbed by the chest wall or confused with systolic expansion of the left atrium; ejection sounds may be aortic rather than pulmonary. Electrocardiographic changes are late, or may be concealed by left ventricular hypertrophy. Radiological changes may be absent.

Although there is a great deal of information about splitting of the second heart sound (recently summarized by Leatham (1964)), the effect of pulmonary hypertension has been strangely neglected. Wood (1952) stated that the second sound in pulmonary hypertension was abnormally closely split, with accentuation of the pulmonary component. We shall show that though this may be correct in a certain situation, no such generalization can be made.

SUBJECTS AND METHODS

Selection of Patients. The records of all patients in whom right heart catheterization had been performed at St. George's Hospital were examined, and all those with a mean pulmonary artery pressure of 20 mm.Hg or more above the sternal angle at rest were included in the survey if a phonocardiogram had been recorded. In a few patients, the quality of the recordings was inadequate for inclusion in the study. A small number of patients was excluded because of complex congenital cardiac defects (especially those with transposition of great vessels), and aortic valve disease or systemic hypertension, as the intensity of the aortic closure sound might be affected. The number of patients with the Eisenmenger syndrome was relatively small, and case records of patients with this diagnosis who had attended the National Heart Hospital were also included in the series if they had been fully investigated, i.e. cardiac catheterization and phonocardiography. No patient was in heart failure, thus excluding a variable cause of prolongation of ventricular systole.

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A total of 116 patients with pulmonary hypertension was studied and divided into 6 main groups (Table I).

Selection of Control Patients. It was soon realized that there was insufficient information about the characteristics of the second heart sound (S_2) in normal subjects, particularly in the older age-groups. The relative intensities of the two components (aortic valve closure (A_2) and pulmonary valve closure (P_2)) in the pulmonary area, the incidence of transmission of P_2 to the mitral area, and the movement of A_2 and P_2 during the respiratory cycle were, therefore, studied in normal subjects grouped by age, for comparison with the patients with pulmonary hypertension (Harris and Sutton, 1968).

There was also insufficient information about S_2 in mitral regurgitation and in intracardiac shunts without pulmonary hypertension. Thus, "control" patients with atrial septal defect (13 patients), ventricular septal defect (13 patients), and slight mitral regurgitation (11 patients) were also investigated, and the results are summarized under the group headings in this paper.

TABLE I
GROUPS OF PATIENTS WITH PULMONARY HYPERTENSION

Groups	No. of patients
Group I: Mitral valve disease with pulmonary hypertension	41
(a) Mitral stenosis	32
(b) Mitral regurgitation	9
Group II: Atrial septal defect with pulmonary hypertension	22
(a) Left-to-right shunting (hyperkinetic pulmonary hypertension)	10
(b) Bidirectional shunting (Eisenmenger situation)	12
Group III: Ventricular septal defect with pulmonary hypertension	20
(a) Left-to-right shunting (hyperkinetic pulmonary hypertension)	7
(b) Bidirectional shunting (Eisenmenger situation)	13
Group IV: Patent ductus arteriosus with pulmonary hypertension	16
(a) Left-to-right shunting (hyperkinetic pulmonary hypertension)	6
(b) Bidirectional shunting (Eisenmenger situation)	10
Group V: Primary pulmonary hypertension	12
Group VI: Chronic respiratory disease with pulmonary hypertension	5

TABLE II
MITRAL STENOSIS

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ —P ₂ relation in pulm. area
			Syst./Diast.	Mean				
F	V.E.	41	35/12	20	3	0.00-0.06*	—	A ₂ > P ₂
F	M.St.L.	45	33/13	20	2	0.00-0.04*	—	A ₂ = P ₂
F	M.H.	50	30/15	20	2	0.00-0.04*	—	A ₂ < P ₂
F	G.H.	57	30/15	20	3	0.00-0.04	—	A ₂ > P ₂
F	M.M.	46	35/12	22	1	0.01-0.05	—	A ₂ = P ₂
F	B.J.	48	40/15	23		0.00-0.04	—	A ₂ > P ₂
F	L.G.	50	45/15	25	4.5	0.02-0.06	—	A ₂ = P ₂
F	J.H.	48	40/18	25	1	0.00-0.03	—	A ₂ = P ₂
M	G.B.	47	40/18	26		0.00-0.03*	—	A ₂ = P ₂
F	L.H.	57	38/15	28	3.3	0.00-0.02	—	A ₂ < P ₂
M	J.M.	57	45/20	28	2	0.00-0.04	—	A ₂ = P ₂
F	A.N.	51	50/22	30	5	0.00-0.02	—	A ₂ > P ₂
M	J.B.	56	45/20	30		0.00-0.04	—	A ₂ < P ₂
F	A.O.	45	50/20	30	3.5	0.00-0.06	—	A ₂ > P ₂
M	W.M.	22	48/18	33	5	0.00-0.02	+	A ₂ < P ₂
M	H.E.	59	48/25	34	7	0.00-0.04	—	A ₂ < P ₂
F	E.S.	52	65/30	36		0.00-0.04	—	A ₂ < P ₂
M	J.F.	54	60/20	38	10	0.00-0.04*	—	A ₂ > P ₂
F	F.H.	52	55/30	40	8	0.00-0.03	—	A ₂ > P ₂
M	G.R.	43	50/25	40	5.5	0.00-0.04	—	A ₂ > P ₂
F	M.C.	25	55/35	40		0.01-0.04	—	A ₂ < P ₂
F	E.B.	42	65/30	41		0.00-0.04	+	A ₂ > P ₂
M	R.K.	49	65/35	45		0.00-0.02	—	A ₂ > P ₂
F	L.McD.	49	65/40	47	5.7	0.00-0.03	—	A ₂ = P ₂
M	A.D.	41	70/55	47	15	0.00-0.04*	—	A ₂ > P ₂
M	J.B.	54	85/45	50	7	0.00-0.03	—	A ₂ = P ₂
M	G.McL.	39	70/30	50		0.00-0.04	—	A ₂ > P ₂
M	G.T.	53	125/30	58		0.00-0.05	—	A ₂ < P ₂
F	J.G.	32	110/40	65		0.00-0.06	+	A ₂ > P ₂
M	T.L.	57	110/50	70	9.3	0.00-0.02*	—	A ₂ = P ₂
M	H.P.	54	115/40	75	7.5	0.00-0.04	—	A ₂ = P ₂
M	A.Y.	43	135/65	95	21	0.04-0.06*	—	A ₂ = P ₂

* Patients in sinus rhythm. Q—A₂ fixed throughout respiratory cycle.

There were no "control" patients with mitral stenosis or patent ductus arteriosus with normal pulmonary artery pressure, because catheterization had not been performed in such patients.

Method of Investigation. Following clinical, electrocardiographic, and x-ray examination, each patient had phonocardiography carried out with simultaneous high frequency recordings (Leatham, 1952) from the pulmonary and mitral areas: the record carried a time-marker, electrocardiogram, and respiratory trace. Usually an external carotid artery reference trace was recorded simultaneously by means of an air-filled cuff and a linear manometer and amplifying system (Robinson, 1963). The paper speed was 100 mm./sec., and the photographic recorder responded well to frequencies up to 800 cycles/sec. All recordings were made during continuous respiration.

All phonocardiograms were taken with the patient reclining at 30°-40°, and the following measurements were made over three respiratory cycles. Respiration was never halted.

1. The width of expiratory splitting of S₂.
2. The width of inspiratory splitting of S₂.
3. The movement of A₂ and P₂ using the onset of electrical activity (Q) as the reference point. These time intervals were measured to the nearest 0.01 sec.
4. The relative intensity of A₂ and P₂ in the pulmonary area was measured and graded:

- (i) A₂ greater in amplitude than P₂ (A₂ > P₂)

- (ii) A₂ equal in amplitude to P₂ (A₂ = P₂)

- (iii) A₂ smaller in amplitude than P₂ (A₂ < P₂).

5. The presence or absence of P₂ in the mitral area.

Right heart catheterization had been performed in all patients, with measurement of the pulmonary artery pressure at rest in relation to the sternal angle; in most the pulmonary capillary ("wedge") pressure was also measured. Cardiac output was estimated by the Fick principle, and pulmonary flows in patients with intra-cardiac shunts by the method of Friedlich, Bing, and Blount (1950).

RESULTS

Group I. Mitral Valve Disease with Pulmonary Hypertension

(a) *Mitral Stenosis* (32 patients aged 22-59 years). In all patients the diagnosis was confirmed at operation. The phonocardiographic characteristics of S₂ are shown in Table II, and an example is given in Fig. 1. Mean pulmonary arterial pressure ranged from 20 to 95 mm.Hg at rest, and pulmonary vascular resistance ranged from 1 to 21 units at rest in the 22 patients in whom cardiac output had been measured.

In expiration, S₂ was single in 28 patients, and in only one patient, who had right bundle-branch block with delay in activation of the right ventricle confirmed by a prolonged Q-RV upstroke time, was S₂

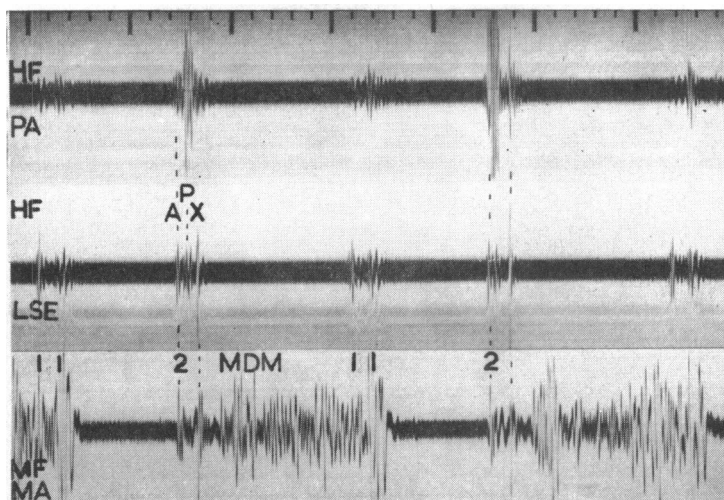


Fig. 1.—Mitral stenosis with pulmonary hypertension (pulmonary arterial pressure 54/24 mm.Hg, pulmonary vascular resistance 5 units). Simultaneous high frequency (HF) phonocardiograms from the pulmonary area (PA), 4th space left sternal edge (LSE), and medium frequency (MF) mitral area (MA). Separation of second heart sound (2) into aortic valve closure (A), and pulmonary valve closure (P) during inspiration with P greater than A in PA but not transmitted to MA. Split first sound (11), opening snap (X), and mitral diastolic murmur (MDM) also recorded. Time markers at 0.20 and 0.04 sec.

wider than 0.02 sec. in expiration. In inspiration, the width of splitting of S_2 varied from 0.02–0.06 sec., and it was found that the level of the pulmonary arterial pressure did not affect this width, as can be seen in Table II where the cases are arranged in order of increasing pulmonary arterial pressure. All patients in sinus rhythm maintained a constant $Q-A_2$ interval throughout respiration.

The A_2-P_2 ratio in the pulmonary area showed that in 8 patients (25%) A_2 was less in intensity than P_2 , in 11 patients (34%) A_2 equalled P_2 , and in 13 patients (41%) A_2 was greater than P_2 . There were no correlations between the levels of the pulmonary vascular resistance and pulmonary arterial pressure, and the A_2-P_2 intensity ratio. P_2 was recorded in the mitral area in 2 patients in whom A_2 was greater than P_2 in the pulmonary area, and in one in whom P_2 was greater than A_2 .

Comment. In mitral stenosis with pulmonary hypertension, whether slight or great, S_2 splits normally on inspiration, but is abnormal in two respects. First, the splitting of S_2 in inspiration is due solely to delay in P_2 , while $Q-A_2$ remains constant in those patients with a constant diastolic filling time (i.e. sinus rhythm), whereas in normal subjects it is unusual for $Q-A_2$ to be fixed throughout respiration. Secondly, despite the lack of correlation between the level of pulmonary arterial pressure or pulmonary vascular resistance and the $A_2:P_2$ ratio in the pulmonary area, P_2 was equal to

or greater than A_2 in 59 per cent of patients, while in normal subjects in the same age-group (22–59 years) P_2 was never equal to or greater than A_2 . Transmission of P_2 to the mitral area, which never occurred in normals in this age-group, was found in only 3 patients with mitral stenosis.

(b) *Mitral Regurgitation* (9 patients aged 5–57 years). In all patients the diagnosis of dominant mitral regurgitation had been confirmed by left ventricular cine-angiography (Rees, Jefferson, and Harris, 1965). The phonocardiographic characteristics of the group are summarized in Table III. Mean pulmonary arterial pressure ranged from 30–65 mm.Hg at rest, and the pulmonary vascular resistance in 4 patients from 2–13 units.

In 4 patients, S_2 was single in expiration. In 4 others, S_2 was wider than 0.02 sec. in expiration without right bundle-branch block or prolonged $Q-RV$ upstroke time. In inspiration, the width of splitting of S_2 varied from 0.04–0.07 sec. $Q-A_2$ was constant during respiration in all patients in sinus rhythm.

The A_2-P_2 ratio in the pulmonary area showed that in 2 patients A_2 was less than P_2 , in 4 patients A_2 was equal to P_2 , and in 3 patients A_2 was greater than P_2 in intensity. There did not appear to be a correlation between these ratios and the level of the pulmonary arterial pressure. In one patient, in whom A_2 was greater than P_2 , P_2 was recorded in the mitral area.

TABLE III
MITRAL REGURGITATION

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ -P ₂ relation in pulm. area
			Syst./Diast.	Mean				
M	W.L.	57	50/20	30		0-00-0-04	—	A ₂ > P ₂
M	P.F.	53	60/25	37	2	0-02-0-06	—	A ₂ = P ₂
F	P.S.	5	55/25	40		0-03-0-05*	—	A ₂ < P ₂
F	E.P.	37	95/10	55	8-5	0-00-0-04*	—	A ₂ > P ₂
F	D.B.	54	70/50	57		0-00-0-04	—	A ₂ < P ₂
F	L.P.	44	90/35	60	13	0-04-0-04	+	A ₂ > P ₂
M	W.R.	47	90/50	65		0-00-0-05	—	A ₂ = P ₂
F	L.C.	54	110/50	65	13	0-04-0-05*	—	A ₂ = P ₂
F	I.B.	45	100/45	65		0-05-0-07	—	A ₂ = P ₂

* Patients in sinus rhythm. Q-A₂ fixed throughout respiratory cycle.

These findings were compared with those in 11 patients who had a late systolic murmur and presumed slight mitral regurgitation (Wood, 1950; Criley *et al.*, 1966) and normal pulmonary arterial pressure. In 6 of these patients, Q-A₂ remained fixed during respiration, while in the remainder, Q-A₂ shortened in inspiration in the normal way. A₂ was invariably greater than P₂ in the pulmonary area, and was never transmitted to the mitral area.

Comment. The second heart sound of patients with slight mitral regurgitation is normal, apart from a slightly higher incidence of constancy of Q-A₂ throughout respiration. Patients with mitral regurgitation with or without pulmonary hypertension often show wide splitting of S₂ in expiration (greater than 0-02 sec.), rarely recorded in normal subjects in the semi-recumbent position. This has been attributed to shortening of left ventricular systole from the mitral regurgitation (Brigden and Leatham, 1953) rather than to pulmonary hypertension. In 6 out of the 9 patients with pulmonary hypertension, P₂ was relatively increased in relation to A₂ in the pulmonary area, by comparison with normal subjects and those with slight mitral re-

gurgitation. Thus, pulmonary hypertension is likely to be present in a patient with mitral regurgitation if P₂ is of equal or of greater intensity than A₂ in the pulmonary area.

Group II. Atrial Septal Defects

(a) *Atrial Septal Defect with Left-to-right Shunt (Hyperkinetic Pulmonary Hypertension)* (10 patients aged 18-60 years). Three patients in this group had additional anomalous pulmonary venous drainage; one had an ostium primum defect; the remainder had ostium secundum defects. The diagnosis in each patient was established by a significant rise in oxygen saturation at right atrial level, and in some patients angiocardiology was also carried out. Mean pulmonary arterial pressures ranged from 25-65 mm.Hg at rest, and the pulmonary vascular resistance averaged 5 units (Table IV). Arterial oxygen saturation was normal at rest in all patients.

In all patients the splitting of S₂ was at least 0-03 sec. in expiration. In 6 patients, the A₂-P₂ interval remained constant throughout respiration. In 4 patients splitting increased slightly on inspiration because of delay of P₂ greater than A₂: in 3 of

TABLE IV
ATRIAL SEPTAL DEFECT: LEFT-TO-RIGHT SHUNTING (HYPERKINETIC PULMONARY HYPERTENSION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ -P ₂ relation in pulm. area
			Syst./Diast.	Mean				
F	D.W.	49	48/15	25		0-04-0-04	+	A ₂ > P ₂
F*	J.McA.	49	48/15	28	3	0-04-0-04‡	+	A ₂ < P ₂
F†	R.S.	60	50/20	30		0-04-0-04	+	A ₂ < P ₂
M†	J.R.	18	42/20	30		0-04-0-05	+	A ₂ > P ₂
F†	S.C.	53	40/25	35	3	0-03-0-05‡	+	A ₂ = P ₂
F	J.D.	34	70/28	38	7	0-04-0-05	+	A ₂ < P ₂
M	H.D.	57	55/25	36	3	0-03-0-04	+	A ₂ = P ₂
M	P.P.	36	60/30	42	3-4	0-04-0-04	+	A ₂ < P ₂
F	P.D.	37		45	5	0-04-0-04‡	+	A ₂ < P ₂
M	T.E.	50		65	9	0-04-0-04	+	A ₂ < P ₂

* Ostium primum defect.

† Additional anomalous pulmonary venous drainage.

‡ Q-A₂ fixed throughout respiratory cycle; Q-A₂ delays in inspiration in all remaining patients.

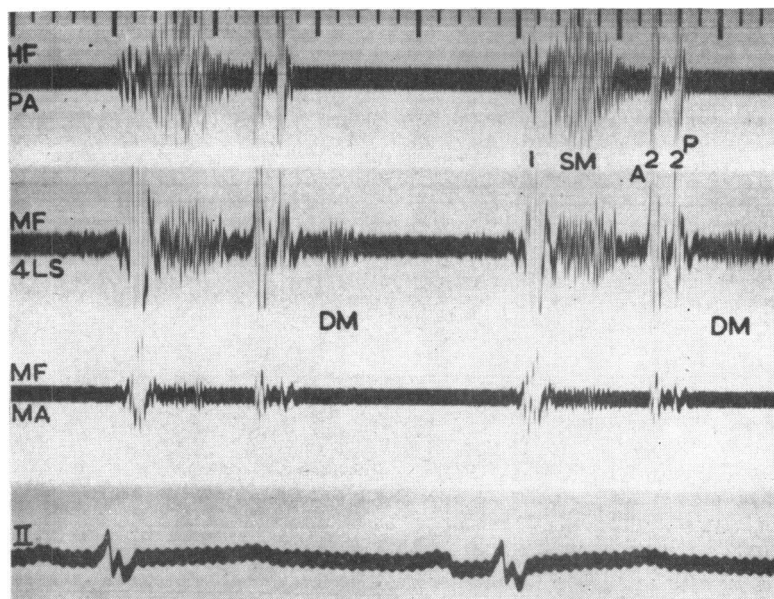


FIG. 2.—Atrial septal defect with left-to-right shunt and without pulmonary hypertension (pulmonary arterial pressure 22/6 mm.Hg, pulmonary vascular resistance 0.5 units). Simultaneous phonocardiograms in pulmonary area, mitral area, and 4th left space (4LS) with the last two at medium frequency (MF). S_2 shows fixed, 0.04 sec. splitting, with A_2 equal in intensity to P_2 in the pulmonary area, and P_2 transmitted to the mitral area. There is an ejection systolic murmur (SM), and a tricuspid flow diastolic murmur (DM). Lead II of electrocardiogram (II).

them the defect was probably small, and partial anomalous pulmonary venous return was present, and in the other it was not excluded. In 7 patients, including the 4 with definite, or likely, additional anomalous pulmonary venous return, the $Q-A_2$ interval increased in inspiration (see Fig. 3), whereas in 3 patients $Q-A_2$ and $Q-P_2$ remained constant throughout respiration. In 13 patients with atrial septal defect and normal pulmonary arterial pressure the characteristics of the splitting of S_2 were similar (Fig. 2).

The A_2-P_2 ratio in the pulmonary area showed that in 6 patients A_2 was less than P_2 , in 2 patients A_2 was equal to P_2 (Fig. 3), and in 2 patients A_2 was greater than P_2 . In all patients P_2 was recorded in the mitral area. In the control group of patients with atrial septal defect and normal pulmonary arterial pressure the $A_2:P_2$ ratio was similar, and P_2 was present in the mitral area in 8 of the 10 patients who had had a phonocardiogram recorded in the mitral area.

(b) *Atrial Septal Defect, Bidirectional Shunting (Eisenmenger Situation)* (12 patients aged 23–74 years). In all patients the diagnosis was confirmed at cardiac catheterization and indicator dye dilution curves demonstrated the presence of a right-to-left

shunt at atrial level. In all patients the arterial oxygen saturation at rest was less than 90 per cent. The mean pulmonary arterial pressure ranged from

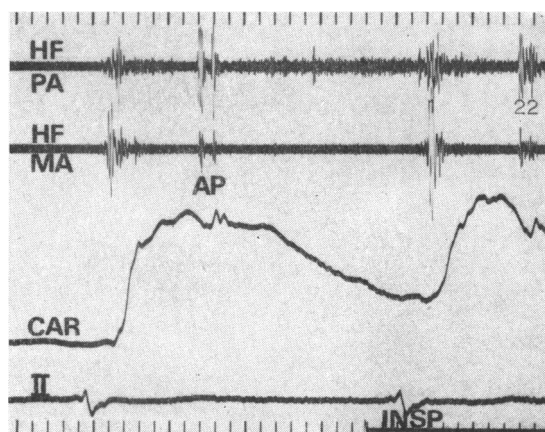


FIG. 3.—Atrial septal defect with left-to-right shunt and pulmonary hypertension (pulmonary arterial pressure 36 mm.Hg, pulmonary vascular resistance 3 units). S_2 shows fixed splitting of 0.04 sec. ($Q-A_2$ and $Q-P_2$ increase simultaneously on inspiration with $A_2=P_2$ in intensity in the pulmonary area.) P_2 is recorded in the mitral area. External carotid artery tracing (CAR) is recorded simultaneously, and inspiration (INSP) is marked.

TABLE V
ATRIAL SEPTAL DEFECT: BIDIRECTIONAL SHUNTING (EISENMENGER SITUATION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ -P ₂ relation in pulm. area
			Syst./Diast.	Mean				
F	B.R.	35	55/25	32	6	0.03-0.04	+	A ₂ < P ₂
M	C.P.	45	75/25	40	9	0.05-0.05	+	A ₂ = P ₂
F	E.K.	32	65/32	44	22	0.06-0.06	+	A ₂ > P ₂
F	D.G.	49		45	7.5	0.06-0.06	+	A ₂ < P ₂
M	G.E.	43		45	7	0.03-0.05	+	A ₂ < P ₂
F	D.K.	39		50	6.6	0.04-0.04	+	A ₂ < P ₂
F	G.C.	34		50	9	0.03-0.04	?	A ₂ < P ₂
M	R.L.	27		50	6	0.04-0.04	+	A ₂ < P ₂
F	B.G.	74	88/30	50	15	0.06-0.06	+	A ₂ < P ₂
F	M.M.	43	120/40	62		0.06-0.06	+	A ₂ > P ₂
F	G.K.	34	110/50	70	20	0.04-0.04	+	A ₂ < P ₂
F	P.M.	23	110/60	75		0.04-0.04	?	A ₂ = P ₂

Q - A₂ delays on inspiration in all patients.

32-75 mm.Hg and pulmonary vascular resistance from 6-22 units (Table V).

In expiration the splitting of S₂ was 0.03 sec. or more in all patients. In inspiration the width of splitting remained constant in 9 of these 12 patients, and widened slightly in the remainder. In all patients, Q-A₂ (and Q-P₂) increased in inspiration (Fig. 4). The width of the splitting did not bear any relation to the level of the mean pulmonary arterial pressure.

The A₂:P₂ ratio in the pulmonary area showed that in 8 patients A₂ was less than P₂ (Fig. 4), in 2

patients A₂ was equal to P₂, and in 2 others A₂ was greater than P₂. In all patients in whom a mitral area phonocardiogram had been recorded, P₂ was present.

Comment. The "fixed" splitting of S₂ in atrial septal defect is one of the most helpful physical findings in making this diagnosis (Leatham and Gray, 1956). This feature remains true, with or without pulmonary hypertension, unless the defect is small, and is explained by simultaneous delay of A₂ and P₂ in inspiration in most instances (Shafter, 1960). The effect of inspiration in increasing the stroke volumes of both ventricles equally has been explained by alteration in the degree of shunting at atrial level (Boyer and Chisholm, 1958; Aygen and Braunwald, 1962), and is frequently found when the shunt is left to right and is invariable when right to left.

The A₂:P₂ ratio in the pulmonary area was abnormal in that P₂ was greater than A₂ in a high proportion of patients with pulmonary hypertension (left-to-right shunt or right-to-left shunt), but the ratio was equally abnormal in 13 patients with atrial septal defect and normal pulmonary arterial pressures. P₂ was almost always heard and recorded in the mitral area in atrial septal defect, irrespective of the presence or absence of pulmonary hypertension, and was probably related both to the increased size of the right ventricle which forms the cardiac apex and to increased intensity of P₂. Although the simple A₂-P₂ intensity ratio was not helpful in diagnosing pulmonary hypertension in atrial septal defect, a great broadening of P₂, together with dwarfing of A₂, made pulmonary hypertension likely.

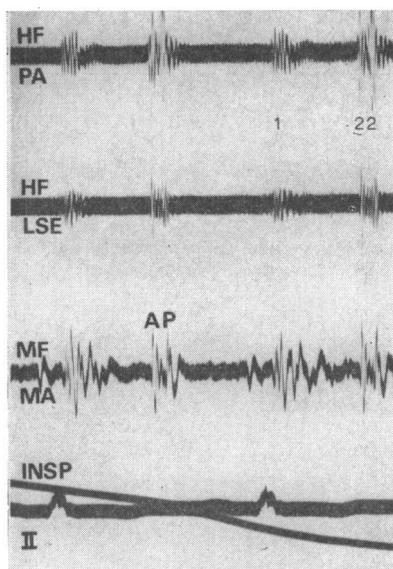


FIG. 4.—Eisenmenger atrial septal defect (pulmonary artery pressure 40 mm.Hg, pulmonary artery resistance 9 units). S₂ shows fixed splitting (0.05 sec.) with P₂ greater than A₂ in the pulmonary area, and P₂ transmitted to the mitral area. Q-A₂ and Q-P₂ delay simultaneously on inspiration. There is no ejection systolic murmur nor tricuspid diastolic murmur.

Group III: Ventricular Septal Defects

(a) *Ventricular Septal Defect with Left-to-right Shunt (Hyperkinetic Pulmonary Hypertension)* (7

TABLE VI

VENTRICULAR SEPTAL DEFECT: LEFT-TO-RIGHT SHUNTING (HYPERKINETIC PULMONARY HYPERTENSION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ -P ₂ relation in pulm. area
			Syst./Diast.	Mean				
F	M.C.	23	43/14	24		0.04-0.06†	—	A ₂ = P ₂
M	P.C.	4	45/15	30		0.01-0.04†	—	A ₂ < P ₂
M*	A.W.	15	50/25	37	5.2	0.00-0.04†	+	A ₂ < P ₂
M	D.B.	3	55/10	40		0.00-0.04†	—	A ₂ = P ₂
F	J.W.	4/12	58/25	40		0.02-0.04†	+	A ₂ < P ₂
M	D.C.	2	80/40	55		0.00-0.02†	+	A ₂ = P ₂
F	D.T.	18		75	5.7	0.00-0.03†	?	A ₂ = P ₂

* Gerbode defect.

† Q-A₂ fixed throughout respiratory cycle.

patients aged 4 months–23 years). The diagnosis was confirmed at cardiac catheterization in all patients, the defect closed in 5, and the pulmonary artery banded in 2. The mean pulmonary arterial pressure at rest ranged from 24–75 mm.Hg (Table VI).

In expiration, S₂ was single or near single in 6 patients, and was split by 0.04 sec. in the seventh in whom there was no right bundle-branch block on the electrocardiogram, and no prolongation of Q-RV upstroke time. In inspiration the width of splitting always increased, varying from 0.02–0.06 sec. Q-A₂ remained constant throughout respiration in all these patients (Fig. 5). In 13 patients with ventricular septal defect without pulmonary hypertension, expiratory splitting was 0.03 sec. or more in 9, and Q-A₂ was fixed in 8 (Fig. 6).

The A₂:P₂ ratio in the pulmonary area showed that A₂ was less than P₂ in 3 patients, and the relative intensities were equal in the remaining 4. P₂ was recorded in the mitral area in 3 patients. In ventricular septal defect without pulmonary hypertension, A₂ was invariably greater than P₂ in the pulmonary area and P₂ was never transmitted to the mitral area.

(b) *Ventricular Septal Defect, Bidirectional Shunting (Eisenmenger Situation)* (13 patients aged 2–40 years). The diagnosis was confirmed in all patients at cardiac catheterization. Mean pulmonary arterial pressure at rest ranged from 45–93 mm.Hg and pulmonary vascular resistance from 6–44 units (Table VII).

A₂ and P₂ could not be separated in any of these patients (Fig. 7). S₂ occupied 0.01–0.02 sec. in all patients so that on auscultation it appeared to be “slurred”. In all patients Q-S₂ increased during inspiration, indicating that A₂ and P₂, fused together, delayed on inspiration. No comment could be made on the relative intensities of A₂ and P₂, nor on the ability to record P₂ in the mitral area, as it was not possible to separate the two components.

Comment. In ventricular septal defect, unlike atrial septal defect, useful information about the pulmonary vascular resistance and the direction of shunting can be obtained from S₂. In a small ventricular septal defect without significant pulmonary hypertension the splitting of S₂ varies from normal in that Q-A₂ may remain constant, and abnormally wide splitting often occurs throughout respiration (with Q-P₂ increasing normally in inspiration): this has been explained by delay in P₂ due to late right ventricular contraction and to a premature A₂ from shortening of left ventricular isometric time (Leatham and Segal, 1962).

In ventricular septal defect with hyperkinetic pulmonary hypertension, the splitting of S₂ remains the same as in ventricular septal defect without

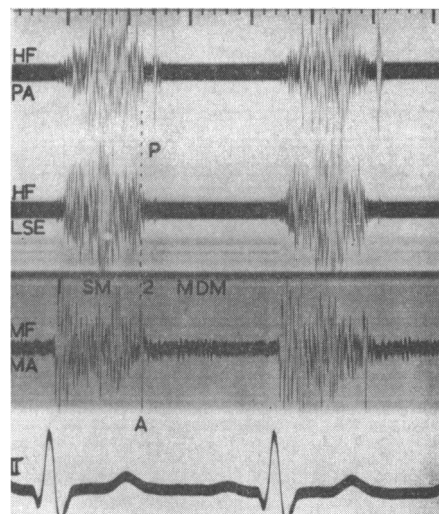


FIG. 5.—Ventricular septal defect with pulmonary hypertension (pulmonary arterial pressure 50 mm.Hg, pulmonary vascular resistance 5 units). S₂ is split by 0.04–0.05 sec. A₂ merges with the pansystolic murmur in the pulmonary area, but is clearly recorded in the mitral area. P₂ is greater than A₂ in the pulmonary area, and not transmitted to the mitral area.

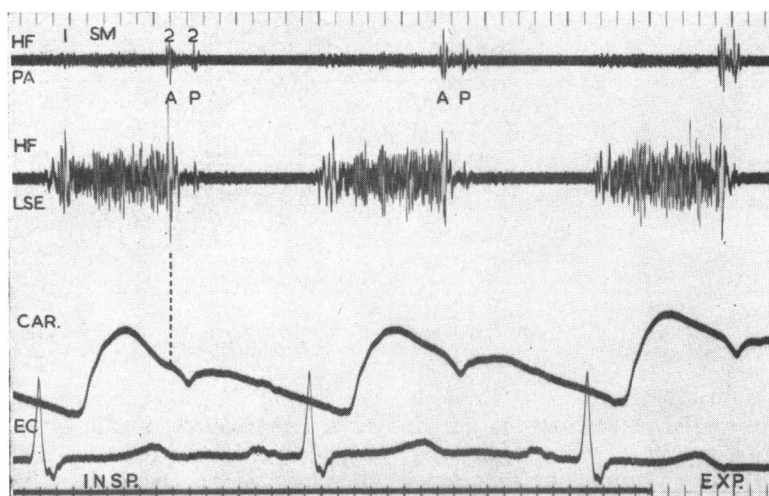


FIG. 6.—Ventricular septal defect without pulmonary hypertension (pulmonary artery pressure 20 mm.Hg, pulmonary vascular resistance 1 unit). S_2 splits from 0.03 sec. in expiration to 0.06 on inspiration. A_2 is greater than P_2 in the pulmonary area.

pulmonary hypertension, except that in expiration S_2 tends to be single, which may be explained by greater overloading of the left ventricle and delay of A_2 from the bigger shunt. In an Eisenmenger ventricular septal defect, however, the two components of S_2 become very close and indistinguishable, both to auscultation and phonocardiography, in all phases of respiration, giving rise to the impression of "slurring". This is associated with identical systemic and pulmonary vascular resistance, for we have noticed that A_2 and P_2 may be asynchronous even in a patient with a single ventricle if systemic and pulmonary resistances are different. During inspiration, the time interval increases between Q and this "slurred" sound (i.e. $A_2 + P_2$).

The $A_2:P_2$ ratio is normal in ventricular septal defect with normal pulmonary arterial pressure. In pulmonary hypertensive left-to-right shunting ventricular septal defect, P_2 becomes relatively increased in intensity, though this may be difficult to determine as A_2 can be drowned in the pansystolic murmur (Fig. 6). In the Eisenmenger situation, it is likely that the intensity of P_2 is also increased, but this is impossible to determine as A_2 and P_2 are inseparable. Transmission of P_2 to the mitral area does not occur in ventricular septal defect with normal pulmonary arterial pressure, occasionally occurs in hyperkinetic pulmonary hypertensive defects, and cannot be determined in the Eisenmenger situation.

TABLE VII

VENTRICULAR SEPTAL DEFECT: BIDIRECTIONAL SHUNTING (EISENMENGER SITUATION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S_2 on expiration and inspiration
			Syst./Diast.	Mean		
F	C.R.	3	68/27	45	7	Single
F	G.B.	6	60/40	48		Single
M	I.E.	38	80/22	60	13	Single
M	G.H.	27	100/45	60	6	Single
M	T.P.	5	80/50	60		Single
F	V.L.	40		70	23	Single
M	V.G.	2	95/55	75	44	Single
M	E.R.	10		78		Single
M	C.T.	7	110/60	80	15	Single
F	J.T.	26		80	27	Single
F	S.G.	21	120/60	80	29	Single
F	A.C.	20	120/75	90	17	Single
F	M.O'D.	3	112/65	93		Single

Q— S_2 delays on inspiration in all patients.

Group IV: Patent Ductus Arteriosus

(a) *Patent Ductus Arteriosus with Left-to-right Shunt (Hyperkinetic Pulmonary Hypertension)* (6 patients aged 7–66 years). The diagnosis was confirmed at cardiac catheterization, and angiocardio-graphy was carried out in some patients mainly to exclude aorto-pulmonary window. The duct was closed in all patients. Mean pulmonary arterial pressure at rest ranged from 45–90 mm.Hg and the pulmonary vascular resistance from 6–14 units (Table VIII).

In 2 patients splitting was normal, and in 2 others was reversed, with P_2 preceding A_2 and delaying on inspiration; in 2 other patients, 2 separate components of S_2 could not be identified in any phase of respiration. In all patients, $Q-A_2$ remained fixed.

In the 4 patients in whom A_2 and P_2 were identified, A_2 was greater than P_2 in the pulmonary area in 3, and equal in amplitude to P_2 in one. In no instance was P_2 recorded in the mitral area.

(b) *Patent Ductus Arteriosus, Bidirectional Shunting (Eisenmenger Situation)* (10 patients aged 6–42 years). The diagnosis was made by the catheter entering the aorta via the ductus in most patients. Mean pulmonary arterial pressures ranged from 63–95 mm.Hg, and pulmonary vascular resistance from 15–32 units (Table IX).

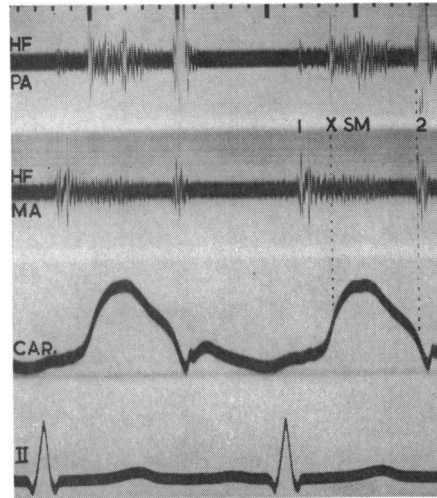


FIG. 7.—Eisenmenger ventricular septal defect (pulmonary artery pressure 60 mm.Hg, pulmonary vascular resistance 6 units). S_2 is slurred but single. $Q-S_2$ varies with respiration. A pulmonary ejection sound (X) and ejection murmur (SM) are shown.

In 6 patients S_2 was single, or nearly single, in expiration, splitting to 0.02–0.04 sec. on inspiration (Fig. 8). In 2 patients expiratory splitting was

TABLE VIII

PATENT DUCTUS ARTERIOSUS: LEFT-TO-RIGHT SHUNTING (HYPERKINETIC PULMONARY HYPERTENSION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S_2 on expiration and inspiration (sec.)	P_2 in mitral area	A_2-P_2 relation in pulm. area
			Syst./Diast.	Mean				
F	M.H.	66	80/35	45		Reversed	—	$A_2 > P_2$
M	D.W.	8	92/50	65	12.6	Single	—	
M	H.P.	11	80/55	70	6.8	Reversed	—	$A_2 > P_2$
F	M.F.	7		80	14	Single	—	
F	J.L.	33		80	11	0.00–0.04	—	$A_2 > P_2$
M	C.B.	15	110/60	90		0.00–0.04	—	$A_2 = P_2$

$Q-A_2$ remained constant during respiration in all patients.

TABLE IX

PATENT DUCTUS ARTERIOSUS: BIDIRECTIONAL SHUNTING (EISENMENGER SITUATION)

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S_2 on expiration and inspiration (sec.)	P_2 in mitral area	A_2-P_2 relation in pulm. area
			Syst./Diast.	Mean				
F	J.E.	6		63	15	0.00–0.03*	+	$A_2 = P_2$
F	M.H.	32		67	20	0.00–0.04*	+	$A_2 < P_2$
F	S.M.	9	80/60	68		0.00–0.04*	+	$A_2 < P_2$
F	A.S.	15	87/50	74	22	0.00–0.03*	+	$A_2 < P_2$
F	S.S.	6	85/60	75		0.00–0.02*	+	$A_2 < P_2$
F	J.C.	22		77	22	Single†	—	
F	M.S.	24	105/70	88	27	0.03–0.05*	+	$A_2 < P_2$
F	B.G.	17	110/80	90	28	Single†	—	
M	J.H.	42	136/63	94	32	0.01–0.04*	+	$A_2 < P_2$
F	D.T.	35		95	15	0.03–0.06*	?	$A_2 < P_2$

* $Q-A_2$ constant throughout respiration.

† $Q-S_2$ increases in inspiration.

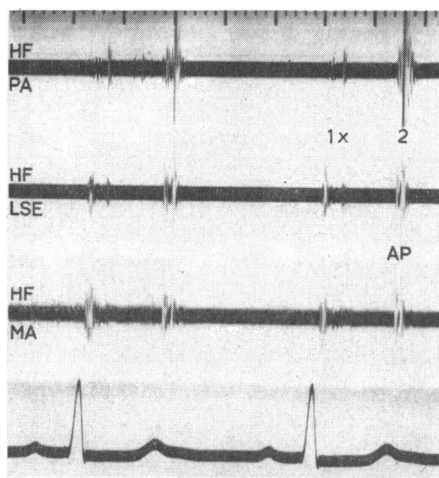


FIG. 8.—Eisenmenger patent ductus arteriosus (pulmonary arterial pressure 88 mm.Hg, pulmonary vascular resistance 27 units). S_2 splits 0.02–0.04 sec., with $Q-A_2$ constant. P_2 is greater than A_2 and transmitted to the mitral area. Ejection sound (X) is recorded.

wider from right bundle-branch block with $Q-RV$ delay. In the remaining 2 patients S_2 was single throughout respiration. In the 8 patients with inspiratory splitting, $Q-A_2$ was constant, so that any respiratory variation was in $Q-P_2$. The 2 patients with a single S_2 showed a delay of $Q-S_2$ on inspiration, as in patients with an Eisenmenger ventricular septal defect, and will be discussed later.

In the 8 patients with splitting, A_2 was less than P_2 in the pulmonary area in 7 and equal in the other: P_2 was always transmitted to the mitral area (there was no phonocardiogram in the mitral area in one patient).

Comment. In patent ductus arteriosus with hyperkinetic pulmonary hypertension, splitting of

S_2 may be physiological or reversed without a distinctive difference from patent ductus arteriosus with normal pressure (Gray, 1956).

In patent ductus arteriosus with bidirectional shunt (Eisenmenger situation), splitting was physiological, apart from $Q-A_2$ remaining constant throughout respiration, with 2 exceptions. In these 2 patients, each with a duct traversed by the catheter, S_2 was single and $Q-S_2$ delayed on inspiration as in an Eisenmenger ventricular septal defect. Review of the catheter data showed a rise of oxygen saturation in the right ventricle in the first patient and in both the x -ray appearance suggested an Eisenmenger ventricular septal defect rather than patent ductus arteriosus (Rees and Jefferson, 1967). In the second patient, however, evidence of the suspected additional ventricular septal defect could not be obtained from the catheter data, but it was subsequently learned that she had died elsewhere, and at necropsy there was a large ventricular septal defect (1.5 cm. in diameter) as well as a duct.

The intensity of P_2 was accentuated, and P_2 transmitted to the mitral area, only in patients with an Eisenmenger situation in this small series.

Group V: Primary Pulmonary Hypertension (12 patients aged 20–66 years).

The diagnosis was based on normal “wedge” pressures and high pulmonary arterial pressure without any evidence of intracardiac shunt. The group included patients in whom thrombo-embolic pulmonary hypertension could not be excluded. Mean pulmonary arterial pressure ranged from 40–80 mm. Hg and pulmonary vascular resistance from 11–48 units (Table X). In expiration, S_2 was split wider than 0.02 sec. in 7 patients, and was single in only one patient. In inspiration, the width of splitting of S_2 varied from 0.02 sec.–0.06 sec. In all patients, $Q-A_2$ remained constant during

TABLE X
PRIMARY PULMONARY HYPERTENSION

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S_2 on expiration and inspiration (sec.)	P_2 in mitral area	A_2-P_2 relation in pulm. area
			Syst./Diast.	Mean				
F	O.S.	64	85/35	40	19	0.03–0.05	+	$A_2 = P_2$
F	B.H.	28		45	11	0.04–0.06	+	$A_2 > P_2$
F	R.S.	41		53	16	0.02–0.04	+	$A_2 < P_2$
F	E.C.	54		55	22	0.03–0.04	+	$A_2 > P_2$
M	J.P.	42		55		0.03–0.03	+	$A_2 < P_2$
F	L.K.	23		65	23	0.00–0.02	+	$A_2 < P_2$
F	W.H.	48		66	16	0.01–0.05	+	$A_2 < P_2$
F	J.B.	21		67		0.04–0.04	+	$A_2 < P_2$
F	J.C.	35		75	48	0.03–0.04	+	$A_2 < P_2$
F	J.M.	33		75	21	0.03–0.04	+	$A_2 > P_2$
F	J.T.	20	150/40	75	31	0.01–0.03	?	$A_2 > P_2$
F	M.L.	66		80		0.04–0.06	+	$A_2 = P_2$

$Q-A_2$ remained constant during respiration in all patients.

respiration, and in most Q-P₂ increased with inspiration (Fig. 9).

In 6 patients, P₂ was greater than A₂ in the pulmonary area, in 2 patients A₂ and P₂ were equal in intensity, and in 4 patients A₂ was greater than P₂. P₂ was found in the mitral area in all patients where a recording was available.

Group VI: Chronic Respiratory Disease with Pulmonary Hypertension (5 patients aged 27–62 years).

Of the 5 patients, 2 had sarcoidosis, one kyphoscoliosis and obstructive airways disease, and 2 obstructive airways disease. The mean pulmonary arterial pressure ranged from 28–75 mm.Hg, and in 2 patients in whom a cardiac output had been measured the pulmonary vascular resistance was 5 and 6 units (Table XI).

In expiration, splitting of S₂ was 0.02 sec. or 0.03 sec. in 4 patients (no right bundle-branch block), and S₂ was single in one. On inspiration the splitting increased to 0.03–0.05 sec. in 4 patients, and this increase was solely due to inspiratory delay of P₂, Q–A₂ remaining constant throughout respiration.

The A₂:P₂ ratio in the pulmonary area showed that A₂ was less than P₂ in all patients. In 4 of the 5 patients a mitral area phonocardiogram was available and showed P₂ to be present.

Comment (Primary Pulmonary Hypertension and Chronic Respiratory Disease with Pulmonary Hypertension). Groups V and VI are considered together as the findings on S₂ are similar. It is usual for S₂ to be split by 0.02 sec. or more in expiration (without right bundle-branch block), a finding which is present in only 2 per cent of normal subjects. This implies that right ventricular systole is prolonged, perhaps as a result of right ventricular dysfunction (Shapiro, Clark, and Goodwin, 1965). In inspiration, Q–A₂ remains constant and Q–P₂ increases in most patients. Occasionally, Q–P₂ also remains constant so that the split is “fixed” throughout respiration, indicating that right ventricular ejection cannot be prolonged in

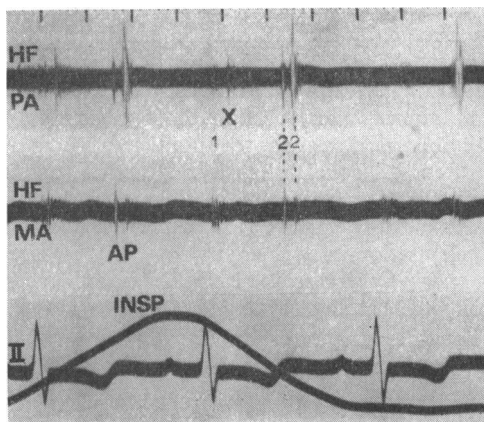


FIG. 9.—Primary pulmonary hypertension (pulmonary arterial pressure 66 mm.Hg, pulmonary vascular resistance 16 units). Splitting of S₂ increases from 0.02–0.05 sec. on inspiration, with P₂ greater than A₂ in the pulmonary area, and recorded in the mitral area. Ejection sound (X) is recorded.

response to an increased systolic volume load on inspiration.

P₂ was greater in intensity than A₂ in the pulmonary area in 6 out of 12 patients with primary pulmonary hypertension and in all the patients with respiratory disease. P₂ was heard and recorded in the mitral area in 11 of the 12 patients with primary pulmonary hypertension and in 4 of the 5 patients with respiratory disease.

Thus, these groups show an unusual degree of splitting of S₂ in expiration, increased intensity of P₂ relative to A₂, and transmission of P₂ to the mitral area.

DISCUSSION

Splitting of Second Sound in Pulmonary Hypertension. Abnormally close splitting of the second heart sound, widely regarded as a sign of pulmonary hypertension, has been shown to apply only to a large ventricular septal defect or single ventricle, and even then the pulmonary vascular resistance has to be raised to systemic levels. The auscul-

TABLE XI
RESPIRATORY DISEASE

Sex	Initials	Age (yr.)	Pulm. art. pressure (mm.Hg)		Pulm. vasc. resist.	Splitting of S ₂ on expiration and inspiration (sec.)	P ₂ in mitral area	A ₂ –P ₂ relation in pulm. area
			Syst./Diast.	Mean				
M	E.S.	62	40/15	28		0.00–0.05	+	A ₂ < P ₂
F	F.P.	48		37	5.5	0.03–0.03	?	A ₂ < P ₂
M	C.M.	51	65/20	37	6.3	0.02–0.05	+	A ₂ < P ₂
M	E.B.	58	70/15	40		0.02–0.03	+	A ₂ < P ₂
M	H.J.	27	105/65	75		0.03–0.04	+	A ₂ < P ₂

Q–A₂ remained constant throughout respiration in all patients.

tory illusion of abnormally close splitting may have been created by the difficulty in hearing the relatively soft A_2 preceding the greatly accentuated P_2 found in many cases of pulmonary hypertension in the pulmonary area, though the two sounds can usually be heard easily at the mitral area where they are often of equal intensity. Another possible reason for the illusion is the likelihood that very wide inspiratory splitting, often present with deep slow respiration in normal subjects, may be rare in pulmonary hypertension, but this aspect was not investigated here.

Though an inspiratory increase in the separation of the two components of the second sound is the rule in pulmonary hypertension without right ventricular failure (except with an interatrial communication or Eisenmenger ventricular septal defect) and is due to inspiratory delay in P_2 as in normal subjects, we were surprised to find the absence of the usual respiratory movement of A_2 in some patients. Though the lengthening of $Q-A_2$ coinciding with expiration is small and sometimes absent in normal subjects, it was entirely absent by ordinary measurements at paper speeds of 100 mm./sec. in patients with mitral stenosis, mitral regurgitation with pulmonary hypertension, and in ventricular septal defect and patent ductus arteriosus with pulmonary hypertension. Normal movement of $Q-A_2$ was often present, however, in patients with minor mitral regurgitation and ventricular septal defect with normal pulmonary pressures. Yet pulmonary hypertension did not seem to be the factor responsible for the fixed $Q-A_2$ interval, since with Eisenmenger ventricular septal defect an inspiratory increase in $Q-A_2$ was present. It might be expected that the normal small inspiratory variations in stroke volume of the left ventricle would be abolished by obstruction to left ventricular filling from mitral stenosis, but they also disappear with severe mitral regurgitation or large left-to-right shunting ventricular septal defect or patent ductus arteriosus. In the latter group, a fixed duration of left ventricular systole ($Q-A_2$ interval) may have been a sign of an abnormal ventricular response to loading, or, in both groups, an increase in pulmonary blood volume might be the explanation. In primary or respiratory pulmonary hypertension the $Q-A_2$ time was also fixed, and while this may have been due to increased blood volume, it may have been caused primarily by reduced inspiratory changes in stroke volume of the right ventricle from failing function.

Thus, despite the lack of help from abnormalities of splitting of the second sound in diagnosing pulmonary hypertension (except in Eisenmenger ventricular septal defect), the inspiratory separation

of the two components not only allows a comparison of relative intensity, but also permits a comparison of the duration of systole of the right and left ventricle in the same heart cycle. Furthermore, the detection of differences in splitting of the second sound remains the only clinical way of differentiating Eisenmenger atrial septal defect, ventricular septal defect, and patent ductus arteriosus, as pointed out by Wood (1958). Wide "fixed splitting" is retained in the Eisenmenger atrial defect (both A_2 and P_2 delay on inspiration), S_2 becomes single with the Eisenmenger ventricular septal defect (fused A_2 and P_2 delay on inspiration), and is physiological with the Eisenmenger patent ductus arteriosus (though $Q-A_2$ is fixed).

In the series of patients with Eisenmenger patent ductus arteriosus, 2 patients had a second heart sound characteristic of an Eisenmenger ventricular septal defect. In one, a step-up of oxygen saturation in the right ventricle and the x -ray suggested an additional ventricular septal defect and in the other, necropsy showed a large ventricular septal defect as well as a duct. Thus it seems that in patients who have both a ventricular septal defect and a patent ductus arteriosus in an Eisenmenger situation, the characteristics of the second heart sound conform to the pattern of the ventricular defect rather than to the patent ductus (Fig. 10). The retention of wide splitting of the second sound in Eisenmenger atrial septal defect may be explained by relative prolongation of right ventricular systole from a combination of pressure loading and volume loading of the right ventricle, the latter factor being absent in Eisenmenger patent ductus arteriosus and less in Eisenmenger ventricular septal defect (no diastolic overloading). In pulmonary hypertensive ventricular septal defect, clear separation of the two components of the second sound excludes an Eisenmenger situation and suggests that surgical closure of the defect may be beneficial.

Intensity and Radiation of P_2 in Pulmonary Hypertension. Since A_2 is larger than P_2 in the pulmonary area in 94 per cent of normal subjects aged 1 to 80 years (Harris and Sutton, 1968), equality of size, or A_2 less than P_2 , usually means an abnormally increased intensity of P_2 , and indicates an atrial septal defect or pulmonary hypertension, and indeed this physical sign was seldom absent in these two situations. Transmission of P_2 to the mitral area is an even more certain abnormality (except in infants), though it did not differentiate normotensive from hypertensive atrial septal defect and was surprisingly infrequent in mitral valve disease. In normotensive or hypertensive atrial septal defect the right ventricle is subjected to a volume overload

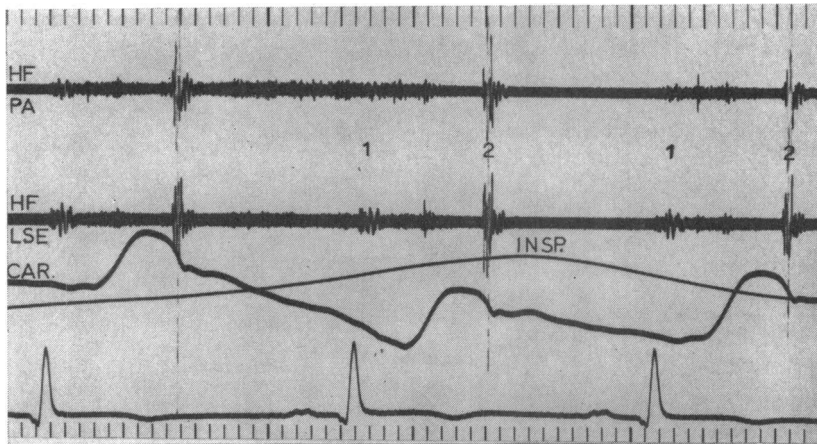


FIG. 10.—Eisenmenger patent ductus arteriosus and ventricular septal defect, not in this series, confirmed at necropsy. S_2 is single and delays on inspiration as with an Eisenmenger ventricular septal defect alone (cf. Fig. 7).

and is thereby greatly dilated; it is lying anteriorly and seems to form the apex of the heart more frequently than with right ventricular hypertrophy from pressure overload. This right ventricular apex in atrial septal defect probably accounts in part for the audibility of P_2 in the mitral area, but another factor is a true increase in intensity of P_2 even in normotensive atrial septal defect, since P_2 was greater than A_2 in the pulmonary area in the majority of cases. This raises the mechanism of increased intensity of P_2 . While the dilated main pulmonary artery of normotensive atrial septal defect may be a factor in bringing the sound nearer to the chest wall, the large pulse pressure in the main pulmonary artery of atrial septal defect, related to the increased stroke volume of the right ventricle, may increase the velocity with which the pulmonary valve closes. Indeed, an increased rate of closure of the pulmonary valve from a waterhammer pulse in the pulmonary artery may be a more important factor in accentuating P_2 than increased pressure of itself, and presumably in pulmonary vascular disease there is increased rigidity of the pulmonary vascular system which is likely to cause a sharp pulse.

SUMMARY

The second heart sound is described in 116 patients with pulmonary hypertension from 6 different causes. Measurements on high frequency phonocardiograms, resembling the findings of auscultation, included the width of splitting and the movements of A_2 and P_2 relative to the Q wave of the electrocardiogram during continuous respiration, the relative intensities of A_2 and P_2 in the pulmonary area, and the transmission of P_2 to the mitral area.

Distinctions are drawn between the findings in the various groups, and a comparison made with normal subjects and patients with similar lesions but without pulmonary hypertension.

In mitral stenosis with pulmonary hypertension, splitting of S_2 is physiological but $Q-A_2$ is constant during respiration in all patients in sinus rhythm. In mitral regurgitation with or without pulmonary hypertension, there may be abnormally wide separation of A_2 and P_2 , and $Q-A_2$ is constant. In mitral stenosis or regurgitation with pulmonary hypertension, P_2 equals or exceeds A_2 in the pulmonary area in two-thirds of cases, a rare finding in normal subjects of similar ages.

In atrial septal defect with pulmonary hypertension, whether left-to-right or right-to-left shunting (Eisenmenger), there is wide "fixed" splitting of the second heart sound with abnormal accentuation of P_2 and frequent transmission to the mitral area. These findings are the same as in atrial septal defect without pulmonary hypertension.

In ventricular septal defect with hyperkinetic pulmonary hypertension and left-to-right shunt, splitting of S_2 is physiological except that $Q-A_2$ remains constant; P_2 equals or exceeds A_2 in the pulmonary area and may be transmitted to the mitral area, unlike normotensive ventricular septal defect. With high pulmonary vascular resistance and right-to-left shunt (Eisenmenger), A_2 and P_2 are fused, delaying together on inspiration.

In patent ductus arteriosus with hyperkinetic pulmonary hypertension and left-to-right shunt, splitting may be physiological or reversed, and A_2 tends to be greater than P_2 . With high pulmonary vascular resistance and right-to-left shunt (Eisen-

menger), splitting of S_2 is physiological apart from $Q-A_2$ remaining constant throughout respiration. P_2 is always greater than A_2 and transmitted to the mitral area.

In primary pulmonary hypertension and pulmonary hypertension secondary to chronic respiratory disease, S_2 is seldom single in expiration, $Q-A_2$ remains fixed during respiration, and $Q-P_2$ increases in inspiration in the absence of right ventricular failure. P_2 is usually louder than A_2 in the pulmonary area, and is transmitted to the mitral area.

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